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LETTERS TO THE EDITOR

Contrast Media Cost Analysis—I

The clinical economic assessment of low versus high osmolality contrast media in angiocardiography by Powe et al. (1) calculated the net costs from three different cost perspectives. They concluded that the cost of side effects associated with high osmolality contrast media partially offset the higher cost of low osmolality contrast media, depending on the cost perspective. Their study represented one of the most comprehensive assessments to date, featuring the cost of four degrees of adverse effects.

Two significant concerns exist with their methods. First, the assignment of adverse event costs may have been skewed by insufficient methodology. The authors used means to represent central tendencies per treatment group. However, in their Table 4, they demonstrated that there were no significant differences between the treatment groups in mean costs per adverse event category. Use of the mean per group, however, assigned a much higher expected cost to the high osmolality group. A more balanced approach would have used the pooled mean cost per adverse event category assigned to both treatment groups. The weighted expected cost of adverse events per group would still have been fairly driven by the significant difference in incidence between treatment groups. The authors partially attempted this approach by using sensitivity analysis to analyze only the pooled cost of severe adverse events. The mild and moderate adverse event categories were much greater in incidence, and the difference between groups was statistically significant.

Second, as pointed out in their Discussion, the costs and effects of prophylactic treatment were not assessed. In the Results, allergic reactions and those associated with cardiac conduction effects (2) were not separated. Estimating that 60% of all reactions to high osmolality contrast media were allergy-mediated, explaining at least 40% of adverse effect costs, use of hydroxyzine (25 mg) and cimetidine (300 mg) prophylaxis (3) ($1.80 average wholesale price) with assumed 80% risk reduction could have decreased the hospital average and hospital differential costs associated with side effects of high osmolality contrast media by one-third. This would have increased the negative differences in hospital average costs to $132 and hospital differential cost to $165.

These two areas provide opportunity for more evaluative reporting of data and the need to study the economic benefit of prophylaxis with effective, inexpensive antihistamines. The comparison of high and low osmolality contrast media without adverse event prophylaxis may be neither clinically nor economically relevant in the near future.

ARTHUR S. ZBROZEK, RPH, MSC, MBA
Departments of Internal Medicine and Family Medicine
University of Texas Medical Branch at Galveston
Jennie Sealy Hospital, D-15
Room 530
Galveston, Texas 77555-0415

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Contrast Media Cost Analysis—II

Powe et al. (1) have attempted to provide the kind of well considered cost analysis needed to bring the debate over use of nonionic contrast media into proper perspective. It has long been debated whether the cost of treating mild and moderate adverse events and the attendant delay in completing procedures totally or only partially offsets the cost advantages associated with the use of an ionic agent. In the present study as in a previously published evaluation (2), Powe et al. argue that the cost of treating adverse reactions after ionic high osmolality contrast media only partially offsets the increased cost associated with the use of low osmolality contrast media. They calculate that the savings realized through lower costs for treating adverse events with low osmolality contrast media offsets ~75% of the average cost to society of use of low osmolality agents and 33% of the hospital's differential cost (low vs. high osmolality contrast media) and conclude that the latter agents are more cost-effective for angiographic procedures in low risk patients. However, a critical reading of their results may prove the opposite to be true.

There are several problems with the assumptions made by Powe et al. in calculating the cost-effectiveness of low versus high osmolality contrast media. 1) The entire exercise is predicated on a comparison of two strategies: universal use of high osmolality contrast media or universal use of low osmolality contrast media. As universal high osmolality contrast media use is inconsistent with well accepted standards of practice in the medical community, this all or nothing approach overemphasizes the potential cost savings attributable to use of these agents in specific patient groups and ignores significant medicolegal issues. 2) The reported costs per procedure are inconsistent with current pricing and dosing regimens for contrast media. Powe et al. report using 212 ml of contrast material per study, whereas the average volume used for these procedures in most hospitals is closer to 130 ml (3). The per-procedure contrast media costs given by the authors are $8 for ionic and $215 for nonionic contrast media, with a cost differential of $207. However, today 200 ml of an ionic agent sells for ~$8, whereas the list price for a 150-ml vial of the nonionic Isovue-370 is ~$138.

With current pricing, the average procedure using the nonionic agent would need to involve >230 ml to approach the per-procedure cost cited by the authors. Clearly, this figure is inconsistent with current dosage patterns. A similar analysis with today's prices and an average per-procedure volume of 150 ml would result in a cost differential between low and high osmolality contrast media of $130 ($138 minus $8). If the incidence of adverse reactions and treatment costs ($92 for low, $249 for high osmolality contrast media) were kept constant, and current contrast media list prices were substituted, use of low rather than high osmolality contrast media could provide a cost savings of $27/study from a societal perspective ($230 for low vs. $257 for high osmolality contrast media), and could offset the hospital's differential cost for low osmolality contrast media by

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>50% ($67/$130). Because many larger hospitals purchase contrast media below list price through various contracts, the reduction in the hospital's differential cost would likely be even greater.

Numerous other factors must be considered when selecting a contrast medium for use in an angiographic procedure. For example, although the analysis of Powe et al. considers the costs incurred, it fails to estimate the opportunity cost or potential loss of revenue by the hospital or physician, or both, due to the increased average time treating adverse reactions in patients given high osmolality contrast media. Other important perspectives omitted from the authors' analysis include those of the patient, physician and staff. A recent study by Hopper and Matthews (4) demonstrated that when low risk patients were given a choice of contrast media as part of an informed consent procedure, nearly half of them opted for low over high osmolality contrast media, even if they were required to pay a cost differential of $100 to $150. In that study, 63% of the low risk patients surveyed felt the choice of contrast media should be left to the individual patient. Another recent study, by Debatin et al. (5), demonstrated that physicians would be inclined to use low osmolality contrast media universally if given the choice. That study showed that when physicians were allowed to decide within certain guidelines which patients were at high risk for an adverse reaction, over time they expanded the definition of a high risk patient and increased their use of low osmolality contrast media.

The report by Powe et. al. is an analysis of data previously published in the *New England Journal of Medicine* (6). Although the authors carefully documented information regarding costs incurred, the data used for both analyses are compromised by the extensive screening of potential study participants. Only 26% of the cardiac catheterization patients examined at Johns Hopkins during the study period (505/1955) were enrolled in the study because of numerous preselection criteria, among which were refusal of the patient to give informed consent, unwillingness on the part of the physician to enroll patients, a clinical determination that low osmolality contrast media was warranted, the likelihood of another contrast-enhanced study within 48 h, patient history of contrast reaction or preexisting renal insufficiency. Even given these enrollment biases, the incidence of mild and moderate adverse events was more than three times higher with high than with low osmolality contrast media. In addition, the average per-patient cost of treating reactions was much greater than in the high than in the low osmolality contrast media group. In a trial with randomized, consecutive patient enrollment, it is likely that the incidence of adverse events and the per-patient treatment costs of adverse events in the high osmolality contrast media group would be even higher in comparison with the low osmolality contrast media group.

In this study (6), as in previous comparative studies, the single greatest risk factor, and the only one totally controlled by the physician, was the choice of contrast medium. The study showed that even in patients at very low risk, adverse events were three times more frequent among patients given high osmolality contrast media. The study also showed that the cost of treating adverse reactions in can be significantly higher in a high than in a low osmolality contrast media group. Despite significant protocol biases in favor of high osmolality contrast media, the analysis of Powe et al. demonstrated that the differential cost to the hospital of using low osmolality contrast media may be reduced by >50% when the cost of treating adverse reactions is considered. Considering the actual price and volume of contrast media used today, universal use of low osmolality contrast media for angiocardiographic procedures may be cost-effective from a societal point of view. These findings lend additional support to the argument that factors other than the list price of low osmolality contrast media need to be considered when deciding which type of contrast media to use for angiocardiographic procedures.

Ultimately, regardless of any cost differential, the patients' welfare should be the primary consideration. As the 1993 ACC guidelines on the use of contrast media (7) indicate, individual patients in consultation with their physicians are best suited to make the decision regarding the use of high or low osmolality contrast media for an angiographic procedure.

ADEOYE Y. OLUKOTUN, MD, FACC
Squibb Diagnostics
P.O. Box 4500
Princeton, New Jersey 08540-4500

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Reply

Zbrozek raises two issues concerning our economic analysis of low versus high osmolality contrast media in diagnostic angiocardiography. The first concerns the most appropriate estimate of the cost of adverse reactions. Our analysis protocol was designed to compare the cost (from three perspectives) of high versus low osmolality contrast media–induced adverse reactions of any severity and contrast material costs. In our baseline analysis, we used the mean costs that we observed for high and low osmolality contrast media–induced reactions. After examining the frequency and costs of adverse reactions by subgroups defined by severity level, it became evident that the magnitude of the offset of the difference in material cost related to adverse reactions was driven by level 4 (severe) adverse reactions. We, therefore, examined the sensitivity of our results to the cost of level 4 adverse reactions. This post-hoc analysis showed an estimated 15% offset of the difference in material cost between high and low osmolality contrast media when pooled level 4 costs were used. The observed costs within each severity level were higher among patients receiving high than among patients receiving low osmolality contrast media. Although, the differences in the mean cost of adverse reactions of a given severity by type of contrast media were not statistically significant, our power to detect a true difference was low. We believe that the approach we took in our analyses was reasonable. However, our data are presented in sufficient detail to permit others to make their own assumptions, calculations and conclusions, as both Zbrozek and Olukotun have done.

The second issue raised by Zbrozek is that of the impact of